



Patent Application  
Docket No. D-16117 (SP01-081)  
WIT003-0003

*D. Grawance*  
*#8*  
*5/29/03*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Ma Sha and Kathy Youngbear )

Group No. 1743

Serial No.: 09/811,999 )

Examiner: Elizabeth S. Quan

Filed: March 19, 2001 )

For: **MICROPLATE FOR PERFORMING CRYSTALLOGRAPHY STUDIES AND METHODS FOR MAKING AND USING SUCH MICROPLATES**

**AFFIDAVIT UNDER RULE 1.132**

Dr. Ma Sha does say as follows:

That I am the New Products Manager of the Life Sciences Division at Corning Inc and have been actively working in the field of protein purification, protein biochemistry and protein crystallization since 1986 (see professional vitae--Exhibit A).

That I am a co-inventor of the aforementioned Patent Application.

That in my opinion the pending Claims 1, 10 and 37 in the aforementioned Patent Application contain subject matter that was not taught or disclosed in the references cited by the Examiner in the Office Action dated March 13, 2003.

That in my opinion the commercial success of a microplate sold by Corning, Inc. which has the limitations recited in pending independent Claims 1 and 37 is indicative of the patentability of those claims and their associated dependent claims. This microplate has grossed \$101,000 in 2002 and \$54,282 so far in 2003.

The microplate sold by Corning, Inc. is referred to as "Corning® 96 Well Protein Crystallization Plate" (see advertisement in Exhibit B). As can be readily seen in the advertisement, the Corning® 96 Well Protein Crystallization Plate contains elements that correspond with the elements recited in pending independent Claims 1 and 37. Namely, Corning® 96 Well Protein Crystallization Plate includes a frame that has a plurality of wells formed therein where each well includes a first well having a relatively small

reservoir with a concaved bottom and a second well having a relatively large reservoir positioned near the relatively small concaved reservoir of the first well, wherein the first well and the second well overlap one another (see Claim 1).

That in my opinion the commercial success of the Corning® 96 Well Protein Crystallization Plate is due in part to the presence of the small reservoirs which have concaved bottoms wherein the concaved shape helps to automatically center a deposited protein solution and reagent solution so that the resulting protein crystals can be easily viewed by the researcher. In contrast, the prior art microplates have small wells with flat bottoms in which the protein solution and reagent solution tend to migrate towards the corner or edges of the small well which makes it difficult for the researcher to view the resulting protein crystal (see page 9, lines 6-24 in the patent application).

That in my opinion the fact that one company has copied important characteristics of the present invention namely a protein crystallography microplate that has small reservoirs with concaved bottoms and have made and sold this microplate is further support that the pending independent Claims 1, 10 and 37 are patentable.

The company that is currently making and selling microplates which are covered by pending Claim 10 is C.A. Greiner & Sohne Gesellschaft m.b.H. (Greiner). Greiner is making and selling a microplate known as the "CrystalQuick standard Profile-Round Bottom Plate" (see advertisement in Exhibit C).

As can be seen in the advertisements shown in Exhibit C, the Greiner microplate contains elements that correspond with the elements recited in the pending independent Claim 10. Namely, each protein crystallography microplate has a frame that includes a plurality of wells formed therein, wherein each well has a first well including a relatively small reservoir having a substantially concaved bottom for receiving a protein solution and a reagent solution and a second well including a relatively large reservoir for receiving a reagent solution that has a higher concentration than the reagent solution within the first well, wherein the protein solution and the reagent solution within the first well interact with the reagent solution within the second well via a vapor diffusion process which enables the formation of protein crystals within the first well, wherein said first well and said second well are adjacent to one another. (emphasis added) (see Claim 10).

That in my opinion Greiner began making and selling their round protein well microplates after 5 to 6 representatives from this company attended Corning workshops in Swaziland where Corning released the details of the design, function & prototypes of the Corning® 96 Well Protein Crystallization Plate back in the summer of 2001 during a MIPTECH Microplate meeting in Europe. Due to the close competitive nature in the crystallization microplate field, I recall that two of the representatives from Greiner that attended my workshop were Dr. Gunther Knebel (Director of Product Development & Marketing) and Mr. Robert G. Brino (VP of Product Development).

That in my opinion the commercial success of Corning® 96 Well Protein Crystallization Plate coupled with the fact that a competitor--Greiner--copied the present invention are indicative of the patentability of independent Claims 1, 10 and 37 and their associated dependent claims.

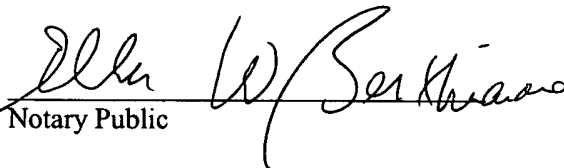
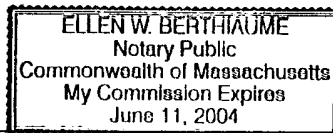
Further I sayeth not.



Dr. Ma Sha

State of MA §  
County of Middlesex § ss.:

On this 14th day of May 2003, before me, a Notary Public in and for the State and County aforesaid, personally appeared, Ma Sha known by me to be the person of the above name who signed and sealed the foregoing instrument, and acknowledged the same to be his own free act and deed.

  
Notary Public

My Commission Expires:

## **PATENTS & PUBLICATIONS**

### **CORNING LIFE SCIENCES:**

- Megan Wang & Ma Sha, "Multiwell plate lid with vents" 2002, patent filed in US, Europe & Asia
- Ma Sha & Kathy Youngbear, "Microplate For Performing Crystllography studies and methods for making & using such microplates" 2001, patent pending.
- Kathy Youngbear & Ma Sha, "Protein Crystallography Hanging Drop Lid That Individually Covers Each Of The Wells In A Microplate" 2002, patent pending.
- Jiling Peng, Bernice Feuier & Ma Sha, "Peptide or Protein-capturing Surfaces For High Throughput MALDI Mass Spectrometry" 2002, Patent Pending
- Armando Villasefor, Ma Sha; P. Thana M. Browner, "Fast Drops: A High-Throughput Approach for Setting Up Protein Crystal Screens " *BioTechniques* 32:184-189 (January 2002).

### **CIPHERGEN BIOSYSTEMS, INC**

- Jarmo Laine\*, Gerald Kunstle\*, Toshiyuki Obata#, Ma Sha+, and Masayuki Noguchi.\*  
"The protooncogene TCL1 is an Akt kinase co-activator" *Mol Cell*. 2000 Aug;6(2):395-407.
- Dierk J. Hampel, Christine Sansome, Ma Sha, Sergey Brodsky, William E. Lawson, Michael S. Goligorsky  
"Towards Proteomics in Uroscopy: Urine Protein Profiling After Radiocontrast Medium" *Kidney International*, 2000.
- Sha, M., Hampel, D., Karavanov, A., and Michael, G., "A CASE OF KIDNEY STONES STUDIED USING PROTEINCHIP™ TECHNOLOGY: PURIFICATION & IDENTIFICATION OF DEFENSIN AND UROMODULIN" (1999) *J. American. Soc. Nephrology.*, Sept. Issue, Vol 10, P 614A.

### **THE ROCKEFELLER UNIVERSITY**

- Sha, M., Levy, T., Kois, P., and Konarska, MM. "Probing of the spliceosome with site-specifically derivatized 5' splice site RNA oligonucleotides". *RNA* 1998 SEP;4(9):1069-1082.
- Konarska MM, Kois P, Sha M, Ismaili N, Gustafson EH, McCloskey J.  
"Probing of ribonucleoprotein complexes with site-specifically derivatized RNA's".  
*RNA Biochemistry and Biotechnology* 1999; 229-240.

### **HARVARD MEDICAL SCHOOL**

- Gilbert, B., Sha, M., Wathen S. T, and Rando, R. R "RNA aptamers that specifically bind to a K Ras-derived farnesylated peptide", *Bioorganic & Medicinal Chemistry*. 5(6):1115-22, 1997 June.

### **CITY UNIVERSITY OF NEW YORK**

- Sha, M., Balasta, M. L., and Goss, D. J. "A Fluorescence Study of the Interaction of Wheat Germ Initiation Factor 4B with Models of the 5'-terminus of mRNA" (1994) *J. Biol. Chem.* **269**, 14872-14877.
- Sha, M., Wang, Y., Xiang, T., Heerdon, A. V., Browning, K. S., and Goss, D. J. "Interaction of Wheat Germ Protein Synthesis Initiation Factor eIF-(iso)4F and its Subunits P28 and P86 with m<sup>7</sup>GTP and mRNA Analogues" (1995) *J. Biol. Chem.*, **270**, 29904-29909.
- Sha, M., Ferré-D'Amaré, A. R., Burley, S. K., and Goss, D. J. "Anti-cooperative Biphasic Equilibrium Binding of Transcription Upstream Stimulatory Factor to Its Cognate DNA Monitored by Protein Fluorescence Changes" (1995) *J. Biol. Chem.* **270**, 19325-19329.

- Wang, Y., Sha, M., Ren, W. Y., Heerdon, A. V., Browning, K. S., and Goss, D. J. "pH-Dependent and Ligand Induced Conformational Changes of Eucaryotic Protein Synthesis Initiation Factor eIF-(iso)4F: A Circular Dichroism Study", Biochimica et Biophysica Acta. (1996, Oct. 17) **1297 (2)**: 207-13.

## **PRESENTATIONS**

Exceptional presentation skills, well-recognized & utilized by CIPHERGEN as well as Corning.

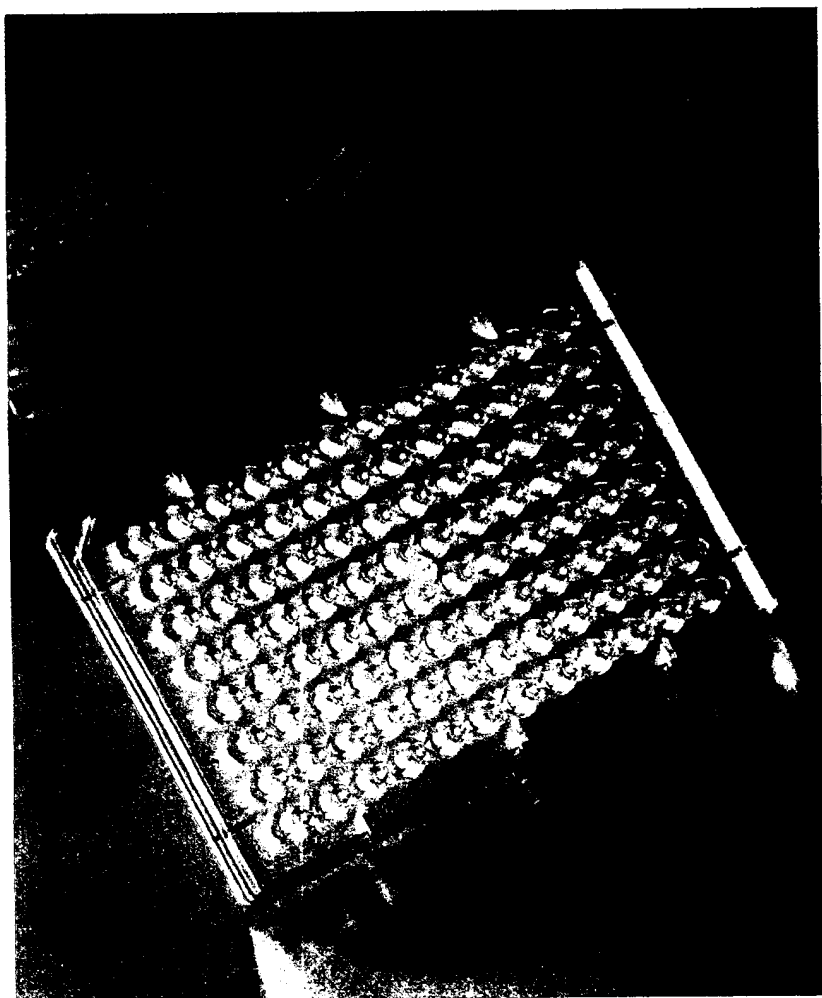
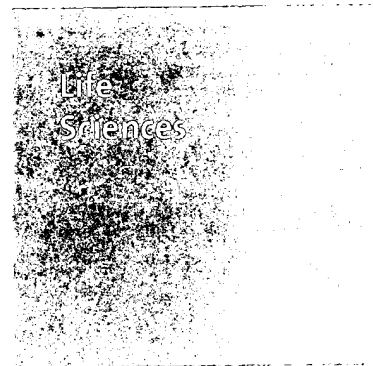
**Over a hundred presentations** at national, international meetings (Switzerland, Japan, Holland, China, USA) as well as other academia institution and big pharmaceutical companies such as: Biophysical Society, American Society of Biochemistry and Molecular Biology, American Chemical society, RNA society, American Soc. Nephrology, Merck, Roche, HMR, Wyeth-, Schering-Plough, Cornell Med., MSKCC, Albert Einstein Med. College, Harvard Med. School, Avon, PHRI, UMDNJ.

## **OTHER ACTIVITIES**

### **Member:**

- Biophysical Society of America.
- Sigma Xi, The Scientific Research Society.
- The American Association for the Advancement of Science (AAAS).
- The American Society of Biochemistry and Molecular Biology (ASBMB).
- ACA: American Crystallography Association.
- SBS: Society of Biomolecular Screening.

# Corning® 96 Well Protein Crystallization Plate



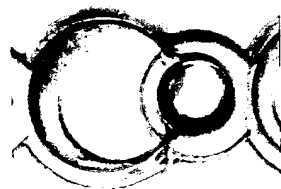
## ***Introducing the Corning Protein Crystallization Plate for Advancing Structural Proteomics***

- ▷ Designed for high throughput protein screens using the sitting-drop format
- ▷ Made of an advanced optically clear polymer that assures precise crystal visualization
- ▷ Features 96 large reservoir wells with corresponding protein wells
- ▷ Maximum volume of 210  $\mu\text{L}$  for the reservoir well and 10  $\mu\text{L}$  for the protein well
- ▷ Recommended working volume of 25 to 125  $\mu\text{L}$  for screening reagents
- ▷ Compatible with robotic equipment for automation

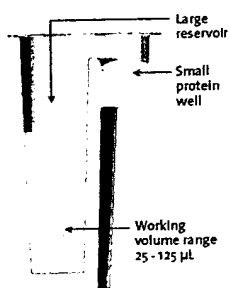
## Advantages of the Corning® Protein Crystallization Plate

The Corning plate is composed of an advanced polymer with properties that make it far superior to polystyrene and polypropylene for high throughput protein crystallography.

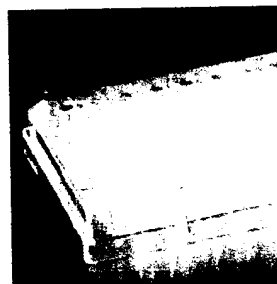
- ▷ **High chemical resistance** to commonly used solvents, including acetone, acetic acid, butanone, ethanol, isopropanol, methanol, DMSO, nitric acid (65%), sulphuric acid (40%), hydrochloric acid (36%), and ammonia solution (33%).
- ▷ **Low background polarization** provides high optical clarity. Protein crystals are easily viewed under polarized light with minimal background interference.
- ▷ **Low water absorption** prevents loss of protein drop volume.



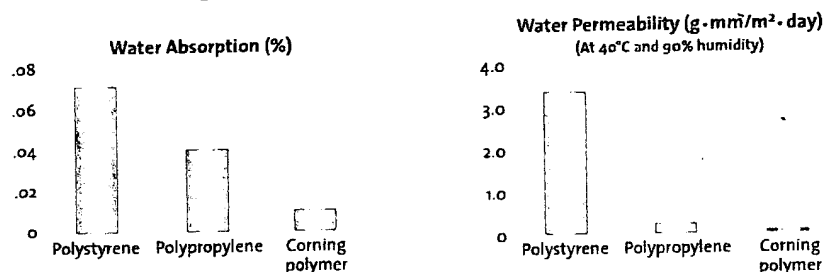
Unique well design (top view)



Cross-section of the crystallization chamber



Corning Universal Optical Sealing Tape



### Other Key Benefits

- ▷ Novel merged well design provides efficient vapor space for the protein crystallization.
- ▷ Conical bottom protein well provides better centering of the protein drop.
- ▷ Footprint and well spacing meet microplate industry standards for automation.
- ▷ Compatibility with 8- and 12-channel pipettors makes manual set ups 10 times faster.

### Corning Universal Optical Sealing Tape

This high optical quality tape is ideal for microscopic observation of protein crystals, minimizes evaporation of well contents, and prevents cross-well contamination. It is suitable for use between -70 and 110°C and is compatible with aqueous solutions and organic solvents.

### Reference

Villaseñor, A., Sha, M., Thana, P., and Browner, M. 2002. Fast drops: A high-throughput approach for setting up protein crystal screens. *BioTechniques* 32:184-189. (Reprints are available from Corning under Corning Literature Number ALSP-AN-019).

### Ordering Information

Cat No.	Description	Qty/Pk	Qty/Cs
3773	96 Well Crystallization Plate, Non-sterile, Without Lid	10	50
6575	Universal Optical Sealing Tape	100	100

For additional product and application information, and a complete listing of our International Offices and Distributors, visit our website: [www.corning.com/lifesciences](http://www.corning.com/lifesciences). All other inquiries please call 1.978.635.2200.

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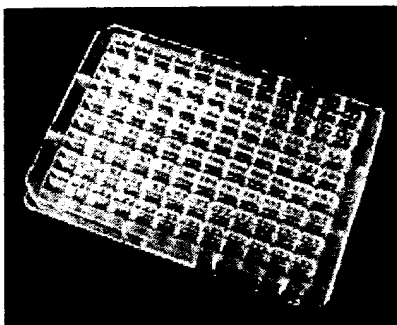
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About Us

Products -&gt; Crystallization Plates and Accessories -&gt; CrystalQuick Standard Profile - Round Bottom Plate

Fast Find... 

## CrystalQuick Standard Profile - Round Bottom Plate



96 well plate for sitting drop vapor diffusion protein crystallization. The plate is designed in the standard microplate format with 8 vertical wells versus 12 horizontal wells. Well shape is square. Within each well is a rectangular reagent reservoir with a capacity of 200 microliters, although 100 microliters is a typical reagent volume for the reservoir. Adjacent to the reagent reservoir is an elevated rectangular platform containing 3 round drop positions. Each drop position is concave with a maximum drop volume of 3 microliters. With 3 drop positions per reagent well, the CrystalQuick Round Bottom is especially useful for screening multiple samples per reagent reservoir or one sample with multiple ligands, inhibitors, or crystallization additives/detergents. The 9 mm center to center pitch between reagent wells makes the CrystalQuick Round Bottom Plate compatible with a wide range of fully automated liquid handling work stations as well as 8 and 12 channel hand pipets. The vertical wells are labeled A-H and the horizontal wells are labeled 1-12. The reservoir well bottoms are frosted. The drop area bottoms are optically clear. At the center top and bottom edge of the plate is a frosted tab which is amenable to automated plate handling devices or grabbers. The plates are stackable. The plate is conveniently sealed with the Hampton Research ClearSeal advanced sealing film. The advanced sealing film is a transparent polyolefin film with clear pressure sensitive silicone adhesive. The film is pre-cut to perfectly fit 96 well crystallization plates and is complete with two 1 centimeter wide, perforated end tabs which make handling and positioning the film easy, without the fear of fingerprints getting into the viewing field. The film has superior optical properties compared to other films. The low tack to touch adhesive means the film does not stick to fingers, gloves, benchtops, or plates until pressure is applied to the film. The ClearSeal film applicator is a small hand-held applicator that can be used to create a consistent film seal across the entire crystallization plate.

### Ordering Info

This plate is useful for the following:

- ☐ Hanging Drop
- ☐ Sitting Drop
- ☐ Sandwich Drop
- ☐ MicroBatch
- ☒ Other: 96 Well Sitting Drop Plate for high throughput screening.

This plate can use the following accessories:

- ☐ 22mm Circle Cover Slides
- ☐ 22mm Thick Circle Cover Slides
- ☐ 22mm Square Cover Slides
- ☐ 22mm Thick Square Cover Slides
- ☐ 18mm Circle Cover Slides
- ☒ Crystal Clear Sealing Tape
- ☒ ClearSeal Film

**Catalog Number: HR3-281**  
**Description: CrystalQuick Standard Profile - Round Bottom Plate**  
**Quantity: 40 plate cas**

**Catalog Number: HR3-283**  
**Description: CrystalQuick Standard Profile - Round Bottom Plate**

EXHIBIT C



**Quantity: 10 plate sampler**

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**Special Sealing Film and Applicator:**

ClearSeal Flim

ClearSeal Film Applicator

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